(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No:	:	10/659,367	Confirmation No.: 3017
Applicant	:	Fei CHEN et al.	
Filed	:	September 11, 2003	
Title	:	DEVICE FOR ANALYSING ANALYTE COMPOUNDS AND USE THEREOF	
Examiner	:	Gary W. Counts	
Art Unit	:	1641	
Docket No.	:	60589.000014	
Customer No.	:	25570	

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REQUEST FOR PRE-APPEAL BRIEF REVIEW IN A CONFERENCE PILOT PROGRAM AND SUPPORTING ARGUMENTS

Sir:

Appellants respectfully request that the members of the panel of Examiners ("Panel") who will review this Request for Pre-Appeal Brief Review allow all claims that were finally rejected in the Office Action of December 31, 2007 in the above-identified patent application. Reversal of the rejections is in order because the final rejection contains several factual deficiencies and fails to establish *prima-facie* case of unpatentability of Appellants' claims.

Claims 1-5, 7-20 and 22-70 are pending in the application. Since claims 34-67, 69 and 70 are withdrawn from consideration, claims 1-5, 7-20, 22-33 and 68 have been examined. All examined claims have been rejected for alleged obviousness as follows:

1) Claims 1-3, 5, 9-13, 20, 22-25, 28, 30-33 and 68 over Good et al. (US Patent 6,194,224) (Good), in view of Wei et al. (US 2003/0119203) (Wei) or Robinson et al. (US 5,726,064) (Robinson);

2) Claim 4 over Good and Wei or Robinson in view of Polzius et al. (U.S. Patent 6,130,097) (Polzius) or Schlipfenbacher et al. (U.S. Patent 5,160,486) (Schlipfenbacher);

3) Claims 7 and 8 over Good and Wei or Robinson in view of Davis et al. (U.S. Patent 6,352,862) (Davis);

4) Claims 14-16 over Good, Wei, or Robinson in view of Lee et al. (WO 02/04671) (Lee);

5) Claim 17 over Good and Wei in view of Lee, and Henderson et al. (U.S. 2004/0072248) (Henderson);

6) Claims 18 and 19 over Good and Wei or Robinson in view of Frushour et al. (US 2003/0059951) (Frushour);

7) Claims 26, 27 and 29 over Good and Wei or Robinson in view of Sundrehagen (U.S. 6,716,641).

I. Combination of Good, Wei or Robinson is Improper and Would Have Failed To Establish *Prima Facie* Obviousness Of Claims 1-3, 5, 9-13, 20, 22-25, 28, 30-33 and 68.

Good discloses a diagnostic test strip comprising a porous material having a sample receiving zone, a reagent zone containing antibodies labelled with colloid gold particles, and a detection zone containing immobilised molecules of the specified analyte when a membrane of the device is moist. Downstream from the detection zone, the device comprises a control zone which contains an immobilized antibody to the antibody coated on the colloidal gold particles, and which indicates the presence of a sample by a detectable change, e.g., visible change. Col. 3, lines 16-19. As is apparent from column 6, lines 53-67, Good discloses a positive/negative test and does not determine the amount of an analyte. In the above paragraph it is stated that "*...a positive sample will inhibit the formation of a visible line in the test zone...*" and that "*Normally a negative oral fluids sample will produce two colored lines, one in the test zone region and one in the control zone region and a positive oral fluids sample will show only one line in the control zone region.*"

As correctly pointed out in the Office Action, Good fails to disclose a calibration zone, much less a single calibration zone comprising an immobilized binding agent having an affinity for the labelled non-immobilized molecule capable of specifically binding to the analyte to be assayed, as required by Appellants' independent claim 1. Contrary to the assertion at page 3 of the Office Action, Good also fails to disclose a third zone extending between the reagent zone and the test zone comprised of nitrocellulose having pore size of 200 to about 500 nm. Good states that his test zone is made of such material, but does not disclose the material of a zone between the reagent zone and the test zone, referred to as the "third zone" in the Office Action. Good col. 4, ll. 21-24. Good also does not disclose a device for any quantitative analyte measurement, much less for the quantitative determination of an analyte in a sample, wherein the content of the analyte in the sample is calculated from a signal obtained in the test zone and a signal obtained in the calibration zone. Appellants respectfully traverse the assertion in the Office Action that these functional recitations are directed to intended use of the device, and thus, in effect are not considered in determining patentability of Appellants' claims.

Section 2173.05(g) of the MPEP states that:

> A functional limitation must be evaluated and considered, just like any other limitation of the claim, for what it fairly conveys to a person of ordinary skill in the pertinent art in the context in which it is used. A functional limitation is often used in association with an element, ingredient, or step of a process to define a particular capability or purpose that is served by the recited element, ingredient or step. >In *Innova/Pure Water Inc. v. Safari Water Filtration Sys. Inc.*, 381 F.3d 1111, 1117-20, 72 USPQ2d 1001, 1006-08 (Fed. Cir. 2004), the court noted that the claim term 'operatively connected' is 'a general descriptive claim term frequently used in patent drafting to reflect a functional relationship between claimed components,' that is, the term 'means the claimed components must be connected in a way to perform a designated function'. 'In the absence of modifiers, general descriptive terms are typically construed as having their full meaning.' *Id.* at 1118, 72 USPQ2d at 1006.
>
> In a claim that was directed to a kit of component parts capable of being assembled, the Court held that limitations such as 'members adapted to be positioned' and 'portions . . . being resiliently dilatable whereby said housing may be slidably positioned' serve to precisely define present structural attributes of interrelated component parts of the claimed assembly. *In re Venezia*, 530 F.2d 956, 189 USPQ 149 (CCPA 1976).

Thus, all of Appellants' claims limitations must be considered in determining patentability of the claims.

Appellants also traverse the assertion that Wei, Robinson and the remaining references relied upon in the Office Action supply the deficiencies of Good to render obvious Appellants' claims.

First, the assertion at page 12 of the Office Action that Robinson and Wei "...clearly teach the advantages of the incorporation of calibration zone into test strips and thus provide the motivation to combine..." is devoid of

factual support. While both references mention calibration zones, the references discuss operation of their devices, as a whole, but do not single out advantages of the calibration zones. Such disclosed calibration zones are mentioned in the context of the two respective references and there is no indication that the calibration zone(s) can or should be used in any other context. Thus, the combination of Good, Robinson and Wei fails to supply the necessary "...articulated reasoning with some rational underpinning to support the legal conclusion of obviousness" required by *KSR Int'l Co. v. Teleflex Inc.,* 127 S.Ct. 1727, 82 USPQ 2d 1385 (2007). *See* also *Ex parte Smith,* slip op. at 14 (BPAI Appeal 2007-1925, June 25, 2007). Appellants note the Board's statement in *Smith* that *KSR* forecloses an argument that a specific teaching is required to find obviousness. Nonetheless, the Supreme Court also held in *KSR* (and the Board agreed) that obviousness rejections "...cannot be sustained by mere conclusory statements..." *Id.*

Wei discloses a lateral flow device for determining an analyte in a sample using the "sandwich" assaying technique. The lateral flow device comprises a sample pad, a conjugate pad, typically containing probes 41 and probe conjugates 42 in such form that the probe conjugates are available for bonding with an analyte. [0031]. The probe may comprise a microparticle, such as a latex bead. The probe may be covalently reacted with an antibody to form a probe conjugate. [0009]. The probe conjugate may travel to react with an analyte in a lateral flow assay to form a "probe conjugate analyte complex" which binds with a first capture reagent in a detection zone 24 (or detection line), to become an immobilized "sandwich complex" or "sandwich" in a detection area or detection zone 24. [0011], [0034], [0035] and [0047]. The first capture reagent may be any ligand specific binder, e.g., an antibody. [0011] and [0035]. Probes 41 and probe conjugates 42 which are not bound to analyte become mobile through the detection line 24 and continue to the calibration zone 32, which includes two or more (e.g. three, four or more) control lines, e.g., calibration lines 25, 26 and 27. Figures 1, 1A and 1B, [0012] and [0039]. The calibration lines may be preloaded with a second capture reagent, such as a second antibody 47. In the calibration zone the control lines have a predetermined amount of a second capture reagent, which may be configured to "immobilize probe-conjugates or probes" that migrate to the control lines *without analyte.* [0012] (Emphasis added.)

In contrast, as is apparent from Appellants' application, in Appellants' method, enabled by the claimed apparatus, analyte migrates to the calibration zone, as a complex with the labeled antibody, i.e., the complex of the labeled antibody bound to the analyte of the sample, binds to the immobilized binding agent in the calibration zone. Further, Wei's control lines have a "binder" (apparently the same as the second capture reagent), used to bind probe 41 molecules and probe–conjugates. [0036] & [0038] Since the second capture reagent has affinity for the probes (i.e., latex, which may include proteins), it is at least not clear if the second capture reagent has affinity for the probe of the probe conjugate, the antibody of the probe conjugate or the probe conjugate.

The amount of the analyte in Wei may be determined by comparing the intensity level of a detection line 24 generated at the detection zone 31 with the intensity level of the calibration lines to calculate the amount of the analyte present. *See,* e.g., paragraph [0039]. Example 3 indicates that the intensities in the three calibrations lines are 0.54 ng, 5.4 ng and 54 ng analyte, respectively. The concentration of analyte of an unknown sample could then be visually determined by comparing the intensity level of the detection line with the intensity level of the three calibration lines.

However, it is clear that the detection line 24 is significantly and fundamentally different from Appellants' fourth zone. The detection line 24 includes capture reagents, e.g. analyte antibodies, which bind to the probe analyte conjugate complexes. In contrast, Appellants' claimed fourth zone includes the same type of analyte to be assayed or its analogue, which is capable of specifically binding to the non-immobilized claimed molecule (included in the claimed second zone of Appellants' analytical device).

Wei's calibration zone is also significantly different from that of Appellants' because it is at least unclear if the second capture reagent has affinity for the probe, the antibody of the probe conjugate or the probe conjugate. In addition, in Wei's calibration zone there is no complex of the labeled antibody bound to the analyte of the sample which binds to the binding agent in the calibration zone because Wei's probe conjugates or probes have no analyte in his calibration zone.

Since Wei's assay device has a fundamentally different construction than that of Appellants' (at least because of the differences in the calibrations zones of the two devices and because Wei's detection zone contains analyte antibodies, instead of Appellants' analyte or its analogue in the fourth zone), Wei teaches away from Appellants' claims. An obviousness assertion based on the combination of Good and Wei amounts to conclusory statements forbidden by *KSR*.

The albeit improper combination of Good and Wei would have failed to produce Appellants' invention of the rejected claims. The improper combination would have comprised a diagnostic test strip including: a sample receiving zone, a reagent zone containing antibodies labeled with colloid gold particles, a detection zone 24 of Wei containing capture reagents, such as analyte antibodies, which bind to the probe analyte conjugate complexes, and a calibration zone, with three calibration lines, which includes a second capture reagent which binds to the probes and probe conjugates which enter the calibration zone without analyte. The amount of analyte present in the sample would be calculated by comparing intensity levels of the three calibration lines to the detection line.

Such an artificially and improperly obtained diagnostic test strip would have been distinct from and not suggestive of Appellants' claimed invention, at least because it would have lacked the fourth zone containing the same type of analyte or its analogue as in an immobilized state capable of specifically binding to the non-immobilized molecule (used in Appellants' second zone), and because its calibration zone would have been fundamentally distinct from that of Appellants'.

Robinson describes a device for determining a ligand in a sample, similar to that of Wei. In column 3, lines 55-58, it is stated that, for a quantitative method, the number of auxiliary calibration surfaces is preferably greater than one and more preferably greater than or equal to four. Appellants submit that it is known in the art that calibration surfaces are equivalent to calibration zones. The term "single calibration zone" in Appellants' claim 1 means one and no more calibration zones, in spite of the assertion in the Office Action that the transitional phrase "comprising" does not exclude other calibration zones.

Further, Robinson discloses several embodiments, e.g., see column 2, lines 7-67 and column 6, line 66 - column 8, line 44. None of these embodiments includes or suggests the combination of zones and other limitations of Appellants' claim 1.

Some of the competitive assays described by Robinson include a reagent, which is a fluorescently labeled ligand analogue that competes with a ligand present in the sample for binding with an immobilized specific binding partner. For example, see col. 10, l. 19 – col. 17, l. 19, such as col. 12, ll. 1-19.

None of Robinson's embodiments discloses or suggests Appellants' claimed device that includes:

(i) a labeled non-immobilized molecule capable of specifically binding to the analyte;

(ii) a fourth zone (test zone) comprising the same type of the analyte to be assayed or its analogue in immobilized state; and

(iii) a calibration zone comprising an immobilized agent having affinity for the labeled non-immobilized molecule capable of specifically binding to the analyte to be assayed.

In particular, none of the embodiments includes a zone similar to Appellants' fourth zone in conjunction with other recited elements of claim 1.

The Robinson's calibration zone(s) have a construction distinct from and not suggestive of Appellants' claimed single calibration zone. For example, Robinson's calibration zone(s) do not utilize and do not suggest the use of a single calibration zone comprising an immobilized binding agent having an affinity for the labeled non-immobilized molecule capable of specifically binding to the analyte to be assayed, together with the remaining elements of the claimed invention. Additionally, Robinson's disclosure fails to suggest the calculation of the amount of the analyte present in the sample from a signal obtained in the fourth zone and a signal obtained in the single calibration zone, as required by Appellants' claims. Additional details of Appellants' claimed analytical device are discussed at page 15, of the Response and Amendment filed on October 24, 2007.

The combination of Robinson with Good is improper, at least because Robinson and/or Good provide no motivation or suggestion of such combination, except by using Appellants' invention as a hindsight-constructed template to selectively pick from Robinson a calibration zone and superimpose it onto Good's disclosure. Such obviousness analysis is contrary to the law. *Ex Parte Katoh et al,* BPAI Appeal 20071460, Decided May 29, 2007 and *Ex Parte Crawford et al,* BPAI Appeal 20062429, Decided May 30, 2007.

For all the above reasons, claim 1 is patentable over Good, in view of Wei or Robinson. Since all the other rejected claims depend from claim 1, they are also *prima facie* patentable, particularly since they include additional limitations which provide further reasons for their patentability in view of the references of record. Thus, no detailed discussion of the remaining rejections of dependent claims is necessary. The Panel's attention is directed to pages 18-20 of the Response filed on September 11, 2006 regarding such other rejections.

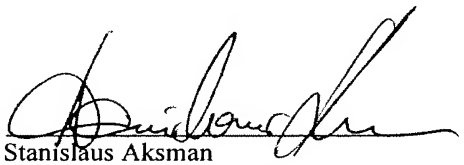
II. Conclusion

In view of the foregoing, it is respectfully submitted that the application is in condition for allowance, and an early indication of the same is courteously solicited. Appellants respectfully request that the Panel hold that all the claims are allowable.

In the event that a variance exists between the amount tendered and that determined by the U.S. Patent and Trademark Office as needed to enter this Request, the Notice of Appeal, or to maintain the present application pending, please charge or credit such variance to the undersigned's Deposit Account No. 50-2478.

Respectfully submitted,

Date: March 21, 2008

By: 
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